

Parameter identification in medical imaging

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Abstract. Positron Emission Tomography is an imaging technique applied in nuclear medicine able to produce images of physiological processes in 2D or 3D. The use of 18F-FDG PET is now a widely established method to quantify tumor metabolism, but other investigations based on different tracers are still far from clinical use, although they offer great opportunities such as radioactive water as a marker of cardiac perfusion. A major obstacle is the need for dynamic image reconstruction from low quality data, which applies in particular for tracers with fast decay like $H_2^{15}O$. The aim of this work is to discuss potential advances in Positron Emission Tomography kinetic models and direct reconstruction of kinetic parameters. We derive a set of differential equations able to represent the kinetic behavior of $H_2^{15}O$ PET tracers during cardiac perfusion. In this model one takes into account the exchange of materials between artery, tissue and vein which predicts the tracer activity if the reaction rates, velocities, and diffusion coefficients are known. The computation of these distributed parameters as a nonlinear inverse problem, which we solve using variational regularization approaches. For the minimization we use Forward-Backward Splitting.

Key Words. Dynamic Positron Emission Tomography, Parameter Identification, Inverse Problems, Imaging, Forward-Backward Splitting, Regularization Theory.

1 Introduction

Positron Emission Tomography is an imaging technique applied in nuclear medicine able to produce images of physiological process in 2D or 3D. In comparison to other imaging techniques with higher spatial resolution, the major advantage of the PET procedure is the high sensitivity and ability for quantitative measurement, making it possible to visualize and to examine specific physiological effects inside the body.

Besides from being a minimally invasive examination and therefore causing less patient discomfort, PET allows the development of better diagnostic imaging, detecting and monitoring the activity of malignant tumors, as well as a better treatment of patients. Many methods to analyze PET data have been developed based on compartmental models such

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as cerebral oxygen utilization [13], neuroreceptor ligand binding [12] and the quantification of blood flow [1, 2, 9, 11].

A short-lived radioactive tracer isotope (γ -type) is injected usually into blood circulation that interacts into the body and after decay it produces a pair of photons that are detected during a PET-scan. Roughly speaking, dynamic PET reconstruction involves the inversion of the Radon Transform K

$$(Ku)(\theta, s; t) = \int_{x:\theta=s} u(x, t) ds(x), \quad u = G(p), \tag{1}$$

with the image u at time t to be constrained by a physiological model, involving physiological parameters $p(x)$ and an operator G that produces an image sequence. Our next step is to create the Inverse Problem associated to this work.

Inverse Problems are focus of current research interest in industrial applications (as the identification of parameters in industrial processes) [4, 5, 7], applications to geophysics [8, 18], tomography and medical sciences (detection of tumors and fractures) [3, 10, 14, 15]. But the biggest disadvantage of working with inverse problems is that the data f are corrupted by noise, especially, because the problem is usually ill-posed in the sense of Hadamard [6]. One problem is called well-posed if it satisfies the conditions of existence, uniqueness and continuous dependence on data. If any of these requirements is not satisfied, the problem is called ill-posed. This instability and ill-conditioning must be overcome if we want to solve the inverse problem satisfactorily. This problem is also transferred to a nonlinear parameter identification problem which we add regularization methods to each biological parameters (that we want to reconstruct) independently and to transform the ill-posed problem in a well-posed.

Thus, we can directly formulate the nonlinear inverse problem

$$\wp(KG(p)) = f,$$

where $f(\theta, y)$ denotes the PET sinograma data and \wp the Poisson statistics. A solution for this inverse problem is given via the minimization

$$\begin{aligned} u \in \arg \min_{u \in \Omega} \left\{ \int_{\Omega} Ku - f \log(Ku) d\sigma(\theta, y) \right\} \\ \Rightarrow u \in \arg \min_{u \in \Omega} \left\{ \int_{\Omega} f \log \left(\frac{f}{Ku} \right) + Ku - f d\sigma(\theta, y) d\sigma(\theta, y) \right\}. \end{aligned} \tag{2}$$

For the minimization we apply a Forward Backward-Splitting method with variable step-size,

$$u_{k+\frac{1}{2}} \in \{u_k - \tau_k \partial_u F(u_k)\}; \quad u_{k+1} \in \{u_{k+\frac{1}{2}} - \tau_k \partial_u H(u_{k+\frac{1}{2}})\}. \tag{3}$$

The first-half step can be realized via the well-known EM iteration to reconstruct the image $u(x, t)$ by

$$u_{k+\frac{1}{2}} = \frac{u_k}{K^*1} K^* \left(\frac{f}{Ku_k} \right). \tag{4}$$

The second half-step is a parameter identification problem, formulated as the constrained optimization problem with added regularization

$$IM(u) + \mathcal{R}(p) \rightarrow \min_p,$$

$$IM(u) = \frac{1}{2} \int_0^T \int_{\Omega} \frac{(G(p) - u_{k+\frac{1}{2}})^2}{u_k} dxdt \text{ for all } x \in \Omega \times [0, T], \quad (5)$$

with some functional IM representing the image reconstruction process and \mathcal{R} denoting the gradient and a-priori regularization functional to each parameter independently (to force well-posedness).

2 Kinetic Modelling

To represent the kinetic behavior of $H_2^{15}O$ PET, during the cardiac perfusion, we use the following Differential Equations [16]

$$\begin{aligned} \frac{\partial C_A}{\partial t} &= -k_0(x)C_A(x, t) - k_1(x)C_A(x, t) + k_3C_V(x, t) \\ &+ \nabla \cdot (V_A(x)C_A(x, t)) + \nabla \cdot (D_A(x)\nabla C_A(x, t)), \end{aligned} \quad (6)$$

$$\begin{aligned} \frac{\partial C_T}{\partial t} &= -k_0(x)C_T(x, t) + k_1(x)C_A(x, t) - k_2C_T(x, t) \\ &+ \nabla \cdot (V_T(x)C_T(x, t)) + \nabla \cdot (D_T(x)\nabla C_T(x, t)), \end{aligned} \quad (7)$$

$$\begin{aligned} \frac{\partial C_V}{\partial t} &= -k_0(x)C_V(x, t) - k_3(x)C_V(x, t) + k_2C_T(x, t) \\ &+ \nabla \cdot (V_V(x)C_V(x, t)) + \nabla \cdot (D_V(x)\nabla C_V(x, t)), \end{aligned} \quad (8)$$

subject to the boundary conditions

$$\begin{aligned} (D\nabla C_{A/T/V} + VC_{A/T/V}) \cdot n &= j_{in} \quad \Gamma \subset \partial\Omega \quad j_{in} = const \cdot V, \\ (D\nabla C_{A/T/V} + VC_{A/T/V}) \cdot n &= C_{A/T/V}V_{out} \quad \partial\Omega/\Gamma. \end{aligned} \quad (9)$$

Here, $C_A(x, t)$, $C_T(x, t)$ and $C_V(x, t)$ represent the radioactive concentrations in the artery, tissue and vein, respectively and $const$ is a constant.

This model differs from others currently found in the literature because here we also consider the contributions due to transport and diffusion. For these, D_A , D_T , D_V , V_A , V_T , V_V are the parameters of diffusion and velocity, in the artery, tissue and vein. All these parameters are written only in function of spatial coordinates, independent of time. The portions k_0C_A , k_0C_T and k_0C_V represent the radioactive decay of the compound. The constants k_1 , k_2 and k_3 represent the exchange of fluids between the artery, tissue and vein.

Considering the above equations, we want reconstruct the image u such that $u(x, t)$ is the sum of the $C_T(x, t)$, $C_V(x, t)$ and $C_A(x, t)$, with

$$p = (k_1(x), k_2(x), k_3(x), D_T(x), D_A(x), D_V(x), V_T(x), V_A(x), V_V(x))$$

and all functions being nonnegative.

3 Discretization of the Differential Equations

We want to discuss in this section the discretization of the differential equations which describe the problem. For this, consider the following system, spatially dependent on x and y and temporal dependent on t :

$$\frac{\partial C}{\partial t} = \nabla((V(x)C) + (D(x)\nabla C)) + \begin{pmatrix} -diag(k_0 + k_1) & k_3 & 0 \\ 0 & -diag(k_0 + k_3) & k_2 \\ k_1 & 0 & -diag(k_0 + k_2) \end{pmatrix} C, \quad (10)$$

where $C = \begin{pmatrix} C_A \\ C_V \\ C_T \end{pmatrix}$, $D = \begin{pmatrix} D_A \\ D_V \\ D_T \end{pmatrix}$ and $V = \begin{pmatrix} V_A \\ V_V \\ V_T \end{pmatrix}$.

We discretize the first time derivative with the operator splitting method using the notation $C(t_k) = C^\tau(k)$. Then we obtain

$$(i) \quad \frac{C^\tau(k + \frac{1}{3}) - C^\tau(k)}{\tau} = \frac{\partial}{\partial x} \left(D_x \frac{\partial C^\tau}{\partial x} \left(k + \frac{1}{3} \right) + V_x C^\tau \left(k + \frac{1}{3} \right) \right), \quad (11)$$

$$(ii) \quad \frac{C^\tau(k + \frac{2}{3}) - C^\tau(k + \frac{1}{3})}{\tau} = \frac{\partial}{\partial y} \left(D_y \frac{\partial C^\tau}{\partial y} \left(k + \frac{2}{3} \right) + V_y C^\tau \left(k + \frac{2}{3} \right) \right), \quad (12)$$

$$(iii) \quad \frac{C^\tau(k + 1) - C^\tau(k + \frac{2}{3})}{\tau} = \mathbf{R} C^\tau(k + 1) \quad (13)$$

where the matrix $\mathbf{R} = \begin{pmatrix} -diag(k_0 + k_1) & k_3 & 0 \\ 0 & -diag(k_0 + k_3) & k_2 \\ k_1 & 0 & -diag(k_0 + k_2) \end{pmatrix}$.

4 Results

4.1 Example of Parameter Identification on Real PET-System

In the following we present an example in order to analyze the reconstruction of the parameters for a specific case. Thus, we use an operator K (16512 x 4225) associated with the PET-real image given by the following figure:

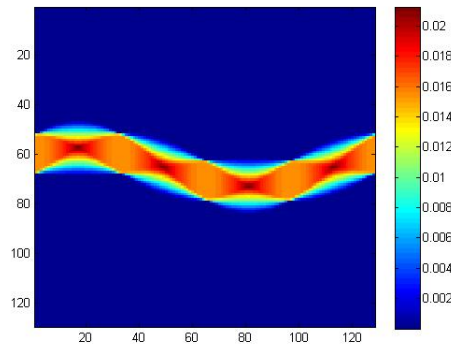


Figure 1: Synthetic image. Forward operator K from real PET scanner

By a given K we are able to produce an image that represents the behavior of real $H_2^{15}O$ -PET-scan data. For this case we use an image 65×65 pixels, in domain Ω . For the radioactive concentration C_A in the artery we use for the initial function

$$C_A(x, y, 0) = \tau(1 - x^2)(N - y)y; \tag{14}$$

with $N = 50$ and the time step $\tau = 3 \cdot 10^{-5}$.

As in the previous example, the radioactive concentration in the tissue and in vein at the beginning are zero and the used method to solve numerically we use the Forward-Backward splitting. All the biological parameters involved are given by the following table.

Here we also evaluate the behavior of radioactive flow when some interval of k_1 e k_2 is

Table 1: Input data for a first real example.

Parameter	Initial Value	$(\cdot)^*$	A-priori Regularization (α)	Gradient Regularization (ξ)
$k_1(*) (1/cm)$	0.9 (0)	0.89	0.017148965	0.0008
$k_2(*) (1/cm)$	0.75 (0)	0.7	0.015801553	0.0001
$k_3 (1/cm)$	0.9	0.85	0.01648965	0.0001
$V_{x_A} (cm/s)$	0.0001	0.1	0.001024495	0.0001
$V_{y_A} (cm/s)$	700	15	1.1000	0.0001
$V_{x_T} (cm/s)$	-50	-5	1.122098745999	0.0001
$V_{y_T} (cm/s)$	0.0001	0.1	0.001024495	0.0001
$V_{x_V} (cm/s)$	0.0001	0.1	0.001024495	0.0001
$V_{y_V} (cm/s)$	700	15	1.1000000001	0.0001
$D_A (cm^2/s)$	$3 \cdot 10^{(-7)}$	$10^{(-3)}$	0.0003344	0.000444
$D_T (cm^2/s)$	$3 \cdot 10^{(-6)}$	$10^{(-2)}$	0.000344	0.000444
$D_V (cm^2/s)$	$3 \cdot 10^{(-7)}$	$10^{(-3)}$	0.0003344	0.000444

equal to zero and therefore, in the above table, the symbol $(*)$ refers to the fact that k_1

and k_2 are not considered constant across the region of interest. When $k_1 = k_2 = 0$ there is no exchange of materials from the artery to the tissue and from the tissue to the vein, and this means that the radioactive concentration (in this region) in the tissue and in the vein are zero.

The following figures refer to the reconstruction of biological parameters for real PET-data:

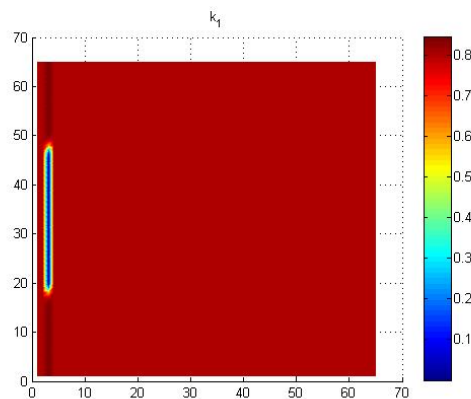


Figure 2: Reconstruction of k_1

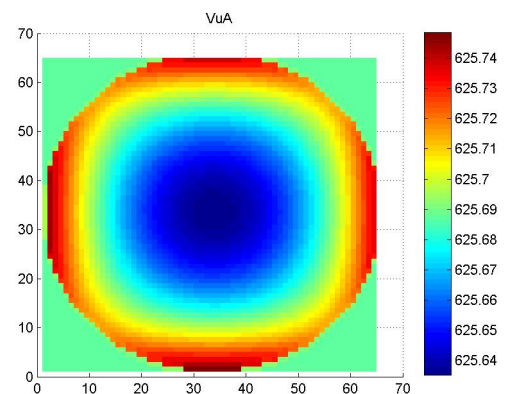


Figure 3: Reconstruction of V_{yA}

5 Conclusion

We have proposed a novel approach for quantitative PET, which is capable of computing parameter reconstructions in presence of flow conditions and we presents the computational tests. The numerical tests presented good accuracy in the reconstruction of the biological parameters when compared to the real values. Future studies aim to add to the proposed model for a new spatial dimension, making it more realistic.

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